Tetrahedron Letters 52 (2011) 5676–5679

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

# Allylation of 1-phenyl-1-propyne with N- and O-pronucleophiles using polymer supported triphenylphosphine palladium complex as a heterogeneous and recyclable catalyst

Yogesh S. Wagh, Dinesh N. Sawant, Kishor P. Dhake, Krishna M. Deshmukh, Bhalchandra M. Bhanage *

*Department of Chemistry, Institute of Chemical Technology, N. Parekh Marg, Matunga, Mumbai 400 019, India*

ARTICLE INFO

*Article history:*
Received 7 July 2011
Revised 16 August 2011
Accepted 18 August 2011
Available online 27 August 2011

*Keywords:*
Allylation
Pronucleophiles
Alkynes
Palladium
Heterogeneous catalyst

ABSTRACT

Simple methodology for the allylation of various N- and O-pronucleophiles with 1-phenyl-1-propyne as an allylating agent, using PS-TPP-Pd (polymer supported triphenylphosphine palladium) as a highly active heterogeneous recyclable catalyst has been developed. The protocol is applicable for a wide variety of hindered and functionalized aromatic amines, alcohols, and carboxylic acids. The catalyst exhibited remarkable catalytic activity for five consecutive recycles.



Allyl amines, allyl ethers, and allyl esters have wide applications in organic synthesis,[1,2] synthesis of biologically active compounds,[3,4] natural products synthesis,[3b] and perfumery industries.[5] These allylated products can be obtained via palladium catalyzed allylation of respective amines, alcohols, and carboxylic acids with various allylating agents such as allyl alcohols, derivatives of allyl alcohols (e.g., allyl acetate, allyl carbonates, allyl triflates, etc.), allenes, or internal alkynes.[6–10] The use of allylating agents like allylic alcohols and their derivatives is not advantageous as it produces stoichiometric amount of side products in the reaction. However, the use of allenes and internal alkynes as an allylating agent is more advantageous, as the allylated products are formed by simple addition reaction of N- and O-pronucleophiles with allenes and alkynes. Among the allenes and alkynes, alkynes are easily available and are also cost-effective. Yamamoto and coworkers[11] reported various homogeneous palladium catalyst such as $Pd(PPh_3)_4$, $Pd_2(dba)_3{\cdot}CHCl_3$ with 2-(dicyclohexylphosphanyl)-2′-(dimethylamino)biphenyl as a ligand, for the allylation of pronucleophiles. Recently, we have reported allylation of various N- and O-pronucleophiles using homogeneous $Pd(OAc)_2$/dppf as catalyst.[12] Homogeneous catalytic systems have several drawbacks like the presence of palladium based impurities in synthesized products, catalyst-product separation, and lack of catalyst reusability. It is noteworthy to mention that such toxic palladium based impurities creates considerable problems in case of pharmaceutical products as the purity of the product is of enormous importance.

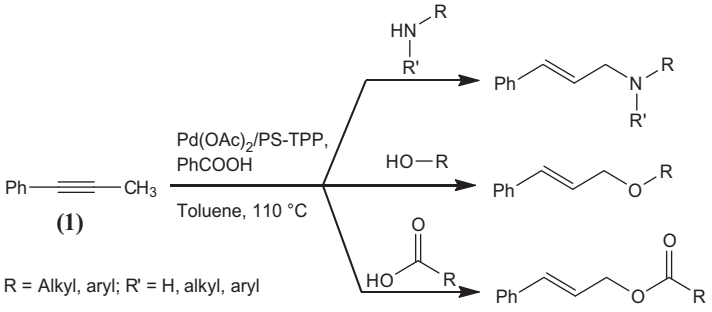
Hence, suitable efforts to anchor such homogeneous complex catalyst which can overcome such limitation of catalyst-product separation and recycle are necessary. In this context, we recently reported an effective heterogeneous catalytic methodology for allylic amination of internal alkynes using polymer supported palladium catalyst.[13] The exploration of developed methodology for the allylation of weaker pronucleophiles such as hindered amines, alcohols, and carboxylic acids still remains the scope of further research. We herein report allylic amination of alkynes using polymer supported palladium catalyst for the allylation of weaker N- and O-pronucleophiles using polymer supported triphenylphosphine palladium complex (PS-TPP-Pd) as a heterogeneous and recyclable catalyst (Scheme 1).

In this work the allylation of 2-methylaniline with 1-phenyl-1-propyne (**1**) as a model reaction using $Pd(OAc)_2$ as a catalyst precursor using polymer supported triphenylphosphine as a ligand and benzoic acid as a co-catalyst was studied. Various reaction parameters such as molar ratio, solvent, temperature, time, and catalyst loading were studied to obtain the best optimized reaction conditions (Table 1).

Molar ratio has always shown a profound effect on the yield of the desired product. Hence, we have studied the effect of different molar ratios of 1-phenyl-1-propyne/2-methylaniline and found that the molar ratio 1:1.2 revealed excellent yields (90%) within 5 h (Table 1, entry 2). Various non-polar organic solvents like tolu-

* Corresponding author. Tel.: +91 22 33612601; fax: +91 22 33611020.
*E-mail addresses:* bhalchandra_bhanage@yahoo.com, bm.bhanage@gmail.com (B.M. Bhanage).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.08.099




**Scheme 1.** PS-TPP-Pd catalyzed allylation of N- and O-pronucleophiles with 1-phenyl-1-propyne.

**Table 1**
Effect of reaction parameters on the allylation of 2-methyl aniline with 1-phenyl-1-propyne (**1**)[a]

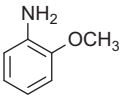
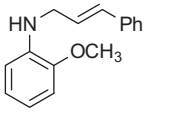
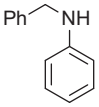
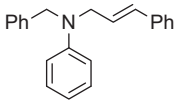
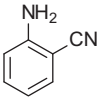
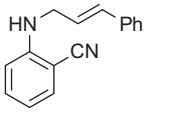
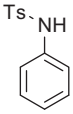
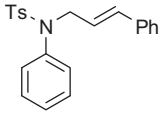
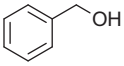
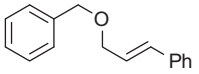
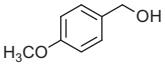
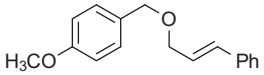
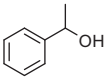
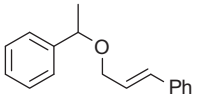
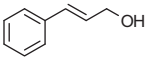
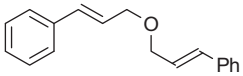
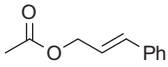
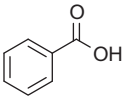
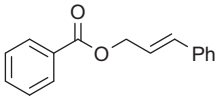
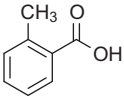
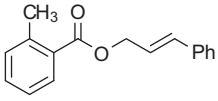
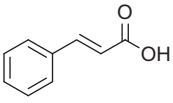
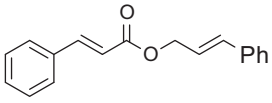
| Entry | Molar ratio | Solvent | Temperature (°C) | Time (h) | Catalyst loading (mol %) | Pd:P ratio | Yield[b] (%) |
|---|---|---|---|---|---|---|---|
| *Influence of molar ratio* | | | | | | | |
| 1 | 1:1 | Toluene | 110 | 5 | 10 | 1:4 | 88 |
| 2 | 1:1.2 | Toluene | 110 | 5 | 10 | 1:4 | 90 |
| 3 | 1.2:1 | Toluene | 110 | 5 | 10 | 1:4 | 86 |
| *Influence of solvent* | | | | | | | |
| 4 | 1:1.2 | Xylene | 110 | 5 | 10 | 1:4 | 60 |
| 5 | 1:1.2 | *n*-Hexane | 70 | 5 | 10 | 1:4 | 05 |
| 6 | 1:1.2 | Cyclohexane | 80 | 5 | 10 | 1:4 | — |
| *Influence of temperature* | | | | | | | |
| 7 | 1:1.2 | Toluene | 100 | 5 | 10 | 1:4 | 78 |
| 8 | 1:1.2 | Toluene | 80 | 5 | 10 | 1:4 | 60 |
| 9[c] | 1:1.2 | Toluene | 120 | 5 | 10 | 1:4 | 90 |
| *Influence of time* | | | | | | | |
| 10 | 1:1.2 | Toluene | 110 | 2 | 10 | 1:4 | 31 |
| 11 | 1:1.2 | Toluene | 110 | 4 | 10 | 1:4 | 76 |
| 12 | 1:1.2 | Toluene | 110 | 6 | 10 | 1:4 | 92 |
| *Influence of catalyst loading* | | | | | | | |
| 13 | 1:1.2 | Toluene | 110 | 5 | 5 | 1:4 | 76 |
| 14 | 1:1.2 | Toluene | 110 | 5 | 15 | 1:4 | 90 |
| *Influence of Pd:P ratio* | | | | | | | |
| 15 | 1:1.2 | Toluene | 110 | 5 | 10 | 1 : 1 | 40 |
| 16 | 1:1.2 | Toluene | 110 | 5 | 10 | 1:2 | 73 |
| 17 | 1:1.2 | Toluene | 110 | 5 | 10 | 1:3 | 76 |
| 18 | 1:1.2 | Toluene | 110 | 5 | 10 | 1:5 | 94 |

[a] Reaction condition: **1** 1-phenyl-1-propyne (5 mmol), **2** 2-methylaniline, $Pd(OAc)_2$ , PS-TPP, benzoic acid (10 mol %), solvent (20 mL).
[b] GC yield.
[c] The reaction was performed in sealed vial.

ene, xylene, cyclohexane, and *n*-hexane were screened and toluene was found to be the best solvent, furnishing excellent yield (90%) (Table 1, entry 2). It was observed that with increase in the reaction temperature from 80 °C to 110 °C, the yield was increased, while further increase in temperature to 120 °C had no significant effect on the yield of the reaction (Table 1, entries 2, 7–9). We further investigated the effect of reaction time and observed that 5 h was sufficient for the reaction (Table 1, entries 2, 10–12). The catalyst loading of 10 mol % was adequate to catalyze the allylation reaction at the palladium: phosphine ratio of 1:5 (Table 1, entries 2, 13–18). We observed that excess amount of phosphine ligand was necessary to stabilize palladium complex for the allylation reaction. Hence, the final optimized reaction conditions are: 1-phenyl-1-propyne (1 equiv), 2-methylaniline (1.2 equiv), toluene at 110 °C, $Pd(OAc)_2$/PS-TPP (10 mol %), ratio of Pd:P (1:5) for 5 h.

Furthermore, the efficiency of developed methodology for the allylation of various N- and O-pronucleophiles was studied (Table 2). Several weaker N-pronucleophiles such as different aniline derivatives containing sterically hindered N-substituted compound (*N*-benzylaniline) as well as electron deficient anilines were subjected for the allylation reaction. We observed that (2-cyanoaniline) and N-sulphonated aniline (*N*-tosylaniline) were well tolerated offering good to excellent yield (82–94%) of the desired allyl amines (Table 2, entries 1–4). Encouraged with the results, we extended our protocol to much weaker pronucleophiles like alcohols and carboxylic acids (Table 2, entries 5–12). Among the O-pronucleophiles screened, the carboxylic acids were found to be much more effective for allylation reaction as compared with alcohols. Benzylalcohol and its derivatives reacted smoothly with **1** providing good yield of the desired product while the reaction of cinnamyl alcohol with **1** offered excellent yield of dicinnamyl ether (90%) as a product (Table 2, entries 5–8). Furthermore, we employed some less nucleophilic O-pronucleophiles, that is, various carboxylic acids such as acetic acid, benzoic acid, *ortho*-toluic acid, and cinnamic acid for the developed methodology. To our delight, all these substrates reacted smoothly to endow excellent yield of their respective allyl esters (Table 2, entries 9–12). In order to avoid the formation of cinnamyl benzoate as a side product in the reaction medium, the reaction of acetic acid and *ortho*-toluic acid with **1** were performed in the absence of benzoic acid (co-cat-

**Table 2**
Allylation of N- and O-pronucleophiles with 1-phenyl-1-propyne[a]

| Entry | Pronucleophile (**2**) | Product (**3**) | Time (h) | Yield[b] (%) |
|---|---|---|---|---|
| 1 |  |  | 6 | 94 |
| 2 |  |  | 12 | 84 |
| 3 |  |  | 12 | 82 |
| 4 |  |  | 18 | 85 |
| 5 |  |  | 18 | 82 |
| 6 |  |  | 18 | 88 |
| 7 |  |  | 18 | 80 |
| 8 |  |  | 18 | 90 |
| 9[c] |  |  | 18 | 85 |
| 10 |  |  | 12 | 92 |
| 11[c] |  |  | 12 | 93 |
| 12 |  |  | 12 | 95 |

[a] Reaction condition: **1** 1-phenyl-1-propyne (5 mmol), **2** N- or O-pronucleophiles (6 mmol), $Pd(OAc)_2$ (10 mol %), PS-TPP (5 equiv to $Pd(OAc)_2$), benzoic acid (10 mol %), toluene (20 mL), temperature (110 °C).
[b] Isolated yields.
[c] Reaction without PhCOOH.

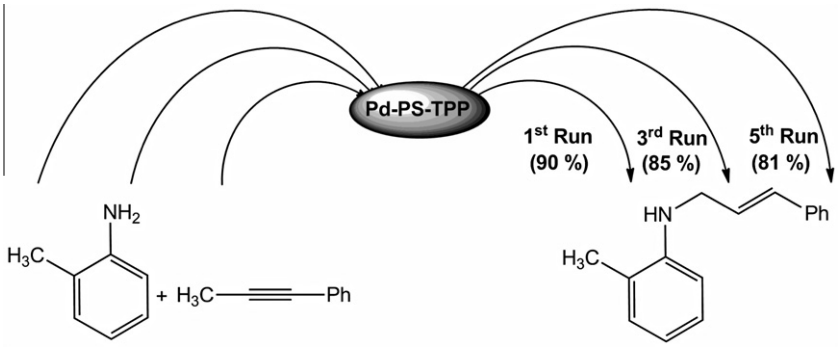



**Figure 1.** Recyclability study for allylation reaction.

alyst) to provide the desired allyl esters with excellent yield. However, the use of benzoic acid as a co-catalyst was essential for the allylation of cinnamic acid as it provided excellent yield of cinnamylcinnamate in the presence of co-catalyst, while reacted sluggishly in the absence of co-catalyst providing only 58% yield.

Though, the hydroxyl group of alcohol is more nucleophilic than the hydroxyl of carboxylic acid, they react sluggishly with alkyne. This observed controversy may be due to the dual role of carboxylic acid as a substrate as well as co-catalyst. Hence, present methodology sounds to be general and economical for the allylation of various structurally and electronically different pronucleophiles such as amines, alcohols, and carboxylic acids with **1** providing good to excellent yields of the desired allylated products.

In addition to make the protocol more economically feasible, the catalytic activity of PS-TPP-Pd was investigated for five consecutive recycles under optimized reaction conditions (Fig. 1). The catalyst was effectively recycled with marginal decline in the catalytic activity for the fifth recycle. The marginal decline in the yield might be due to the handling loss of Pd catalyst. In relation, we performed the ICP-AES analysis of the reaction mixture and observed leaching of the Pd below the detectable level.

In conclusion, we have developed a facile, highly efficient, and common protocol for the allylation of different weak nucleophilic O- and N-pronucleophiles using PS-TPP-Pd complex as a heterogeneous and recyclable catalyst. The present methodology facilitates allylation of weaker nucleophilic amines, alcohols, and carboxylic acids providing good to excellent yield of the desired products. Also, the PS-TPP-Pd complex was recycled for five consecutive cycles without any significant loss in catalytic activity.

## Acknowledgments

The author (YSW) is greatly thankful to the Council of Scientific and Industrial Research (CSIR), India for providing fellowship.

## References and notes

1. For a review on allylic amination, see: (a) Johannsen, M.; Jorgensen, A. *Chem. Rev.* **1998**, *98*, 1689–1708; (b) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199–207; (c) Muller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795–3892.
2. Cheikh, R. B.; Chaabouni, R.; Laurent, A.; Mison, P.; Nafti, A. *Synthesis* **1983**, 685–699.
3. (a) Walsh, C. *Tetrahedron* **1982**, *38*, 871–909; (b) Stutz, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 320–328; (c) Prashad, M. *J. Med. Chem.* **1993**, *36*, 631–632; (d) Michalson, E. T.; Szmuszkovicz *J. Prog. Drug. Res.* **1989**, *22*, 135–149.
4. (a) Reina, M.; Mericli, A. H.; Cabrera, R.; Gonzales-Coloma, C. *Phytochemistry* **1995**, *38*, 355–358; (b) Bergdahl, M.; Hett, R.; Friebe, T. L.; Gangloff, A. R.; Iqbal, J.; Wu, Y.; Helquist, P. *Tetrahedron Lett.* **1993**, *34*, 7371–7374; (c) Genisson, Y.; Mehmandoust, M.; Marazano, C.; Das, B. C. *Heterocycles* **1994**, *39*, 811–818; (d) Jain, P.; Garraffo, H. M.; Spande, T. F.; Yeh, H. J. C.; Daly, J. W. *J. Nat. Prod.* **1995**, *58*, 100–104.
5. Wessermel, K.; Arpe, H. J. *Industrial Organic Chemistry*, 3rd ed.; VCH: New York, NY, 1997.
6. (a) Al-Masumb, M.; Megurob, M.; Yamamoto, Y. *Tetrahedron Lett.* **1997**, *38*, 6071–6074; (b) Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 5421–5424.
7. (a) Yang, S. C.; Hung, C. W. *J. Org. Chem.* **1999**, *64*, 5000–5001; (b) Yang, S. C.; Hsu, Y. C.; Gan, K. H. *Tetrahedron* **2006**, *62*, 3949–3958.
8. Nishikata, T.; Lipshutz, B. H. *Chem. Commun.* **2009**, 6472–6474.
9. (a) Adak, L.; Chattopadhyay, K.; Ranu, B. C. *J. Org. Chem.* **2009**, *74*, 3982–3985; (b) Feuerstein, M.; Laurenti, D.; Doucet, H.; Santelli, M. *Chem. Commun.* **2001**, *1*, 43–44.
10. Moreno, -M. M.; Morral, L.; Pleixats, R. *J. Org. Chem.* **1998**, *63*, 6160–6166.
11. (a) Kadota, I.; Shibuya, A.; Lutete, M. L.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 4570–4571; (b) Lutete, M. L.; Kadota, I.; Shibuya, A.; Yamamoto, Y. *Heterocycles* **2002**, *58*, 347–357; (c) Lutete, M. L.; Kadota, I.; Yamamoto, Y. *J. Am. Chem.* **2004**, *26*, 1622–1623; (d) Patil, N. T.; Wu, H.; Kadota, I.; Yamamoto, Y. *J. Org. Chem.* **2004**, *69*, 8745–8750; (e) Bajracharya, G. B.; Huo, Z.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 4883–4886; (f) Patil, N. T.; Song, D.; Yamamoto, Y. *Eur. J. Org. Chem.* **2006**, 4211–4213.
12. Wagh, Y. S.; Sawant, D. N.; Tambade, P. J.; Dhake, K. P.; Bhanage, B. M. *Tetrahedron* **2011**, *67*, 2414–2421.
13. Wagh, Y. S.; Sawant, D. N.; Tambade, P. J.; Bhanage, B. M. *Eur. J. Org. Chem.* **2010**, 5071–5076.
*General procedure for allylation reaction*: In a typical experimental procedure, 50 mL round-bottomed flask was charged with $Pd(OAc)_2$ (112 mg, 10 mol %), polymer supported triphenylphosphane (PS-TPP; 831 mg, 5 equiv to $Pd(OAc)_2$) and toluene (20 mL) and was stirred for 20 min at 110 °C. The reaction mixture was cooled to rt followed by the addition of 1-phenyl-1-propyne (580 mg, 5 mmol), pronucleophile (6 mmol), and benzoic acid (60 mg, 10 mol %). The resulting mixture was stirred for 5–18 h at 110 °C and was then cooled to room temperature. On completion of reaction, the catalyst was separated by filtration, washed with an excess amount of toluene and dried under vacuum (The dried catalyst can be used as it is for further recycles). The reaction mixture was analyzed using a gas chromatography (Perkin Elmer, Clarus 400) equipped with a flame ionization detector (FID) and capillary column (Elite-1, 30 m × 0.32 mm × 0.25 μm). The crude product was purified by column chromatography (silica gel, 60–120 mesh; petroleum ether/ethyl acetate, 95:05) to afford pure products. All the prepared compounds were confirmed by comparing with their authentic samples and were characterized by GC–MS (Shimadzu QP 2010) , $^1$H NMR (Varian 300 MHz) or (Varian 400 MHz), $^{13}$C NMR (Varian 75 MHz), and HRMS (Bruker daltonics, ESI micrOTOF-Q) analysis.
*Spectral data of selected compounds*:
*N*-Cinnamyl-2-methoxyaniline (Table 2, entry 1). Yield**:** 94% (1048 mg). $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta$ = 7.22–7.39 (m, 5H, Ar), 6.6–6.89 (m, 5H, (4H, Ar and 1H, CH=C*H*-Ph)), 6.35 (td, *J* = 15.76, 5.86 Hz, 1H, $CH_2$–C*H*=CH), 4.42 (br s, 1H, N*H*), 3.95 (dd, *J* = 5.5, 1.46 Hz, 2H, HN–$CH_2$–CH), 3.85 (s, 3H, –$OCH_3$). $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 146.92 (*C*q, Ar), 138.02 (N-*C*q, Ar), 136.99 (Cq, Ar), 131.35 ($CH_2$–*C*H=CH), 128.56 (2*C*H, Ar), 127.46 (*C*H, Ar), 127.27 (CH=*C*H-Ph), 126.36 (2*C*H, Ar), 121.34 (*C*H, Ar), 116.71 (*C*H, Ar), 110.24 (*C*H, Ar), 109.45 (*C*H, Ar), 55.41 (–$OCH_3$), 45.94 (HN–$CH_2$–CH) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 239 (43) [$M^+$], 117 (100), 115 (41), 91 (31), 77 (10), 45 (46), 44 (38). HRMS (ESI$^+$) calcd for ($MH^+$): 240.1388, found ($MH^+$): 240.1387.
*Cinnamyl acetate*: (Table 2, entry 9). Yield: 85% (748 mg). $^1$H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 7.2–7.4 (m, 5H, Ph), 6.65 (d, *J* = 15.76 Hz, 1H, CH=C*H*-Ph), 6.28 (td, *J* = 15.76, 6.23 Hz, 1H, $CH_2$–C*H*=CH), 4.72 (dd, *J* = 6.23, 1.1 Hz, 2H, O–$CH_2$–CH), 2.1 (s, $CH_3$–CO–O, 3H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 170 ($CH_3$–CO–$OCH_2$), 136.26 (*C*q, Ar), 134.25 (CH=*C*H-Ph), 128.65 (2*C*H, Ar), 128.11 (*C*H, Ar), 126.66 (2*C*H, Ar), 123.23 ($CH_2$–*C*H=CH), 65.11 (O–$CH_2$), 21 ($CH_3$) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 176 (28) [$M^+$], 134 (40), 133 (39), 117 (29), 115 (86), 92 (35), 43 (100).
Cinnamyl benzoate (Table 2, entry 10). Yield: 92% (1094 mg). $^1$H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 8.1 (d, *J* = 8.43 Hz, 2H, Ar), 7.2–5.9 (m, 8H, Ar), 6.75 (d, *J* = 15.76, 1H, CH=C*H*-Ph), 6.4 (td, *J* = 15.76, 6.23 Hz, 1H, $CH_2$–C*H*=CH), 5.0 (dd, *J* = 6.23, 1.1 Hz, 2H, O–$CH_2$–CH) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 166.37 (*C*O), 136.25 (*C*q, Ar), 134.27 (Cq-CO, Ar), 133 (*C*H, Ar), 129.67 (2*C*H, Ar), 128.63 (2*C*H, Ar), 128.39 (2*C*H, Ar), 128.1 (CH=*C*H-Ph, Ar), 126.67 (2*C*H, Ar), 123.29 ($CH_2$-*C*H=CH), 65.23 (O–$CH_2$–CH) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 238 (4) [$M^+$], 133 (11), 117 (12), 115 (28), 105 (100), 45 (27).